

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings of claims in the application:

Listing of Claims:

1. (Original) A method of inducing apoptosis in a cancer cell, the method comprising contacting the cell with:
 - i. an anti-DR4 or anti-DR5 affinity agent agonist; and
 - ii. an apoptosis-inducing agent.
2. (Original) The method of claim 1, wherein the agonist is an anti-DR-5 antibody.
3. (Original) The method of claim 2, wherein the anti-DR5 antibody has the binding specificity of an antibody comprising a heavy chain variable region comprising the sequence displayed in Figure 24 or Figure 35 and a light chain variable region as displayed in Figure 25 or Figure 35.
4. (Original) The method of claim 3, wherein the anti-DR5 antibody comprises a heavy chain variable region comprising the sequence displayed in Figure 24 or Figure 35 and a light chain variable region as displayed in Figure 25 or Figure 35.
5. (Original) The method of claim 2, wherein the anti-DR5 antibody is Antibody A (ATCC Deposit No. ____).
6. (Original) The method of claim 1, wherein the agonist is an anti-DR4 antibody.

7. (Original) The method of claim 1, wherein the cell is contacted with an anti-DR4 antibody agonist and an anti-DR5 antibody agonist.

8. (Original) The method of claim 1, wherein the agonist is a humanized antibody.

9. (Original) The method of claim 1, wherein the agonist is a single chain antibody.

10. (Original) The method of claim 1, wherein the agent prevents or reduces the expression of BCL-2.

11. (Original) The method of claim 10, wherein the agent prevents activation of NF κ B.

12. (Original) The method of claim 11, wherein the agent prevents degradation of I κ B.

13. (Original) The method of claim 1, wherein the agent is a proteasome inhibitor.

14. (Original) The method of claim 13, wherein the proteasome inhibitor is selected from the group consisting of PS-341, MG-262 and MG-132.

15. (Original) The method of claim 1, wherein the agent is an inhibitor of an Inhibitor of Apoptosis (IAP) protein.

16. (Original) The method of claim 15, wherein the inhibitor is SMAC or a SMAC mimetic.

17. (Original) The method of claim 1, wherein the cancer cell is a colon cancer cell or a pancreatic cancer cell.

18. (Original) The method of claim 1, wherein the agent is an antagonist of PAK1.

19. (Original) The method of claim 1, wherein the agent is an antagonist of a polypeptide selected from the group consisting of nsurf and JIK.

20. (Original) The method of claim 1, wherein the agent is a siRNA.

21. (Original) A method of inducing apoptosis in a cancer cell in an individual in need thereof, the method comprising,

administering to the individual a therapeutically effective amount of

- i. an anti-DR4 or anti-DR5 affinity agent agonist; and
- ii. an apoptosis-inducing agent.

22. (Original) The method of claim 21, wherein the agonist and the agent are administered separately.

23. (Original) The method of claim 21, wherein the agonist and the agent are administered as a mixture.

24. (Original) The method of claim 21, wherein the agonist is an anti-DR-5 antibody.

25. (Original) The method of claim 24, wherein the anti-DR5 antibody has the binding specificity of an antibody comprising a heavy chain variable region comprising the

sequence displayed in Figure 24 or Figure 35 and a light chain variable region as displayed in Figure 25 or Figure 35.

26. (Original) The method of claim 25, wherein the anti-DR5 antibody comprises a heavy chain variable region comprising the sequence displayed in Figure 24 or Figure 35 and a light chain variable region as displayed in Figure 25 or Figure 35.

27. (Original) The method of claim 25, wherein the anti-DR5 antibody is Antibody A (ATCC Deposit No. _____).

28. (Original) The method of claim 21, wherein the agonist is an anti-DR4 antibody.

29. (Original) The method of claim 21, wherein the cell is contacted with an anti-DR4 antibody agonist and an anti-DR5 antibody agonist.

30. (Original) The method of claim 21, wherein the agonist is a humanized antibody.

31. (Original) The method of claim 21, wherein the agonist is a single chain antibody.

32. (Original) The method of claim 21, wherein the agent prevents or reduces the expression of BCL-2 or UbcH10.

33. (Original) The method of claim 32, wherein the agent prevents activation of NF κ B.

34. (Original) The method of claim 33, wherein the agent prevents degradation of I κ B.
35. (Original) The method of claim 21, wherein the agent is a proteasome inhibitor.
36. (Original) The method of claim 35, wherein the proteasome inhibitor is selected from the group consisting of PS-341, MG-262 and MG-132.
37. (Original) The method of claim 21, wherein the agent is an inhibitor of an Inhibitor of Apoptosis (IAP) protein.
38. (Original) The method of claim 37, wherein the inhibitor is SMAC or a SMAC mimetic.
39. (Original) The method of claim 21, wherein the cancer cell is a colon cancer cell or a pancreatic cancer cell.
40. (Original) The method of claim 21, wherein the agent is an antagonist of PAK1.
41. (Original) The method of claim 21, wherein the agent is an antagonist of a polypeptide selected from the group consisting of UbcH10, nsurf and JIK.
42. (Original) The method of claim 21, wherein the agent is a siRNA.
43. (Original) A physiological composition comprising, a therapeutically effective amount of
 - i. an anti-DR4 or anti-DR5 affinity agent agonist; and

ii. an apoptosis-inducing agent.

44. (Original) The physiological composition of claim 43, wherein the agonist is an anti-DR-5 antibody.

45. (Original) The physiological composition of claim 44, wherein the anti-DR5 antibody has the binding specificity of an antibody comprising a heavy chain variable region comprising the sequence displayed in Figure 24 or Figure 35 and a light chain variable region as displayed in Figure 25 or Figure 35.

46. (Original) The physiological composition of claim 45, wherein the anti-DR5 antibody comprises a heavy chain variable region comprising the sequence displayed in Figure 24 or Figure 35 and a light chain variable region as displayed in Figure 25 or Figure 35.

47. (Original) The physiological composition of claim 46, wherein the anti-DR5 antibody is Antibody A (ATCC Deposit No. ____).

48. (Original) The physiological composition of claim 43, wherein the agonist is an anti-DR4 antibody.

49. (Original) The physiological composition of claim 43, wherein the cell is contacted with an anti-DR4 antibody agonist and an anti-DR5 antibody agonist.

50. (Original) The physiological composition of claim 43, wherein the agonist is a humanized antibody.

51. (Original) The physiological composition of claim 43, wherein the agonist is a single chain antibody.

52. (Original) The physiological composition of claim 43, wherein the agent prevents or reduces the expression of BCL-2 or UbcH10.

53. (Original) The physiological composition of claim 52, wherein the agent prevents activation of NF κ B.

54. (Original) The physiological composition of claim 53, wherein the agent prevents degradation of I κ B.

55. (Original) The physiological composition of claim 43, wherein the agent is a proteasome inhibitor.

56. (Original) The physiological composition of claim 43, wherein the agent is an inhibitor of an Inhibitor of Apoptosis (IAP) protein.

57. (Original) The physiological composition of claim 56, wherein the inhibitor is SMAC or a SMAC mimetic.

58. (Original) The physiological composition of claim 43, wherein the agent is an antagonist of PAK1.

59. (Original) The physiological composition of claim 43, wherein the agent is an antagonist of a polypeptide selected from the group consisting of UbcH10, nsurf and JIK.

60. (Original) The physiological composition of claim 43, wherein the agent is a siRNA.

61. (Currently Amended) An affinity agent with the binding specificity of an antibody comprising a heavy chain variable region comprising the sequence displayed in Figure

24 (SEQ ID NO:4) or Figure 35 (SEQ ID NO:8) and a light chain variable region as displayed in Figure 25 (SEQ ID NO:5) or Figure 35 (SEQ ID NO:10).

62. (Currently Amended) The affinity agent of claim 62 61, which is an antibody comprising a heavy chain variable region comprising the sequence displayed in Figure 24 (SEQ ID NO:4) or Figure 35 (SEQ ID NO:8) and a light chain variable region as displayed in Figure 25 (SEQ ID NO:5) or Figure 35 (SEQ ID NO:10).

63. (Currently Amended) An isolated cell that expresses an antibody of claim 62 with the binding specificity of an antibody comprising a heavy chain variable region comprising the sequence displayed in Figure 24 (SEQ ID NO:4) or Figure 35 (SEQ ID NO:8) and a light chain variable region as displayed in Figure 25 (SEQ ID NO:5) or Figure 35 (SEQ ID NO:10).

64. (Original) A method of inducing apoptosis in a cancer cell, the method comprising contacting the cell with an affinity agent with the binding specificity of an antibody comprising a heavy chain variable region comprising the sequence displayed in Figure 24 or Figure 35 and a light chain variable region as displayed in Figure 25 or Figure 35.

65. (New) The affinity of claim 61, wherein the affinity agent is an antibody.

66. (New) The affinity agent of claim 65, wherein the antibody is a monoclonal antibody.

67. (New) The affinity agent of claim 65, wherein the antibody is a humanized antibody.

68. (New) The affinity agent of claim 65, wherein the antibody comprises the complementarity determining regions of the heavy variable region (SEQ ID NO:8) and light variable region (SEQ ID NO:10) of Figure 35.

69. (New) The affinity agent of claim 65, wherein the antibody comprises the complementarity determining regions of the heavy variable region displayed in Figure 24 (SEQ ID NO:4) and the light variable region displayed in Figure 25 (SEQ ID NO:5).

70. (New) The cell of claim 63, wherein the antibody comprises the complementarity determining regions of the heavy variable region (SEQ ID NO:8) and light variable region (SEQ ID NO:10) of Figure 35.

71. (New) The cell of claim 63, wherein the antibody comprises the complementarity determining regions (CDRs) of the heavy variable region displayed in Figure 24 (SEQ ID NO:4) and the light variable region displayed in Figure 25 (SEQ ID NO:5).

72. (New) The cell of claim 63, wherein the antibody is a humanized antibody.

73. (New) An isolated antibody comprising a complementarity determining region from SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:8, or SEQ ID NO:10.

74. (New) An isolated cell that expresses an antibody comprising a complementarity determining region from SEQ ID NO:4, SEQ ID NO:8, SEQ ID NO:5 or SEQ ID NO:10.